DETAILED ACTION

The examiner notes the receipt of the amendments and remarks received on 11/3/2009 amending claims 1, 2, 8 and 10. Claim 5 has been cancelled. Claims 1-4, 6-14 are free of prior art and are allowable. The claims are renumbered as 1-13. The examiner contacted the Applicants' representative on 1/20/2010 regarding the terminal disclaimer filed by the Applicants for U.S. Patent 7,507,769 (disapproved by the office) to overcome one of the ODP rejections. Applicants' TD filed on 1/20/2010 has been approved by the office on 1/20/2010.

Application Priority

This application claims the benefit of priority to U.S. provisional application No. 60/433,959, filed December 18, 2002.

REASONS FOR ALLOWANCE

Applicants' arguments and the amendment of claim 1 necessitated the withdrawal of rejection of claims 1-3, 6-8, 10, 11-14 under 35 U.S.C. 103(a) as being unpatentable over Jarvis et al. (Applicant cited IDS: U.S. 4,919,937) and Jarvis (Current Therapy in Endocrinology and Metabolism, 280-284) in view of Pujol et al. (Cancer Chemother Pharmacol, 36, 493-498, 1995) and further in view of Fentiman et al. (Br. J. Surg, 75, 845-846, 1988), rejection of claims 1-3, 6-8, 10, 11-14 under 35 U.S.C. 103(a) as being unpatentable over Jarvis et al .(Applicant cited IDS: U.S. 4,919,937) and Jarvis et al. ("Hormonal Therapy of Benign Breast Disease," Senologie et Pathologie

Mammaire.4eme Congres International, Paris 1-4 September 1986, pp. 128-132) in view of Pujol et al. (Cancer Chemother Pharmacol, 36, 493-498, 1995) and further in view of in view of Fentiman et al. (Br. J. Surg, 75, 845-846, 1988), rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Jarvis et al. (Applicant cited IDS: U.S. 4,919,937) and Jarvis (Current Therapy in Endocrinology and Metabolism, 280-284) in view of Pujol et al. (Cancer Chemother Pharmacol, 36, 493-498, 1995) and further in view of Fentiman et al. (Br. J. Surg, 75, 845-846, 1988) as applied to claims 1-3, 6-8, 10, 11-14 above and further in view of Kochinke et al. (U.S. 5,613,958), rejection of claim 4 is rejected 35 U.S.C. 103(a) as being unpatentable over Jarvis et al .(Applicant cited IDS: U.S. 4,919,937) and Jarvis (Current Therapy in Endocrinology and Metabolism, 280-284) in view of Pujol et al. (Cancer Chemother Pharmacol, 36, 493-498, 1995) and further in view of Fentiman et al. (Br. J. Surg, 75, 845-846, 1988) as applied to claims 1-3, 6-8, 10, 11-14 above and further in view of Malet et al (Cancer Research, 48, 7193-7199, 1988). Applicants' have amended claim 1 to indicate that 4-hydroxy tamoxifen is the sole active ingredient in the treatment of mastalgia. The rejection of claim 1 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 18 of copending Application No. 11/249,122 is withdrawn because U.S. Application 11/249,122 has been filed after the instant application. The claims rejected under the doctrine of obviousness-type double patenting over claims 1-9 of U.S. 7,507,769, in view of Mauvais-Jarvis (1988) is withdrawn due to Applicants' filing of the Terminal disclaimer.

The following is an examiner's statement of reasons for allowance:

The claims of the instant application are drawn to a method of treatment of mastalgia comprising administering percutaneously to the breasts of a patient having mastalgia a composition comprising 4-OH tamoxifen as the sole therapeutically active ingredient at a dose of at least 1.5 mg/day of 4-hydroxy tamoxifen.

The closest prior art related to the instant invention is Jarvis et al. (U.S. 4,919,937), Jarvis (Current Therapy in Endocrinology and Metabolism, 280-284), Jarvis et al. ("Hormonal Therapy of Benign Breast Disease," Senologie et Pathologie Mammaire.4eme Congres International, Paris 1-4 September 1986, pp. 128-132), Pujol et al. (Cancer Chemother Pharmacol, 36, 493-498, 1995) and Fentiman et al. (Br. J. Surg, 75, 845-846, 1988).

Jarvis patent teaches a method of treating conditions of the breast including the steps of: forming an aqueous alcoholic gel in which the active ingredient consists of 4-OH tamoxifen and administering percutaneously said aqueous alcoholic gel as an anti-estrogen drug to a breast. The patent teaches that 4-OH tamoxifen acts synergistically with progesterone in treating breast conditions. Also, the reference states that 'The 4-hydroxytamoxifen/progesterone combination is capable of blocking in vitro the activity of estrogens which are factors in cell multiplication, and at the same time of improving the progesterone activity: these are synergistic and complementary actions which are not achieved with the separate administration of each of the constituents of the gel formulation" (col. 4, lines 6-12). Hence it would have not been obvious to one having ordinary skill in the art at the time of the invention to have administered 4-OH tamoxifen (4-OHT) by itself in treating breast conditions. Also, the patent does not teach or

suggest that 4-OHT would be useful in treating a particular benign breast condition such as mastalgia. The amounts of the drug, 4-OH tamoxifen for treating breast conditions is not taught.

Jarvis (Current Therapy in Endocrinology and Metabolism, 280-284), Jarvis et al. ("Hormonal Therapy of Benign Breast Disease," 1986, pp. 128-132) provide a review of proposed therapies, for treating different benign breast disease conditions, including (i) mastalgia, (ii) breast abnormalities (e.g., nodes, fibroadenomas, cysts and fibrocystic disease) and (iii) breast cell multiplication. Mauvais-Jarvis (1986), page 128; Mauvais-Jarvis (1988), page 280, col. 2. The papers discuss several candidates that are "anti-estrogens," including tamoxifen and 4-OHT, but do not teach that any are effective against any benign breast disease condition, let alone mastalgia in particular. The term "benign breast disease" encompasses a number of different benign (non-cancerous) breast conditions including mastalgia, nonproliferative lesions, increased nodularity, fibroadenomas, cysts and fibrocystic disease. See, e.g., Mauvais-Jarvis (1988), Introduction and Table 2. Mastalgia is a particular species of the genus of benign breast disease conditions. Mauvais-Jarvis (1988) demonstrates that a therapeutic agent useful against one benign breast disease condition may not necessarily be useful against other benign breast disease conditions. For example, while percutaneous progesterone was reported to be effective against mastalgia when used alone (75% response rate), it showed only minimal efficacy against nodularity (10% response rate) and no efficacy (0%) against fibroadenomas, cysts, or fibrocystic disease. Mauvais-Jarvis (1988), page 283, Table 2. It would have not been obvious from these studies to one having ordinary

skill in the art that 4-OH tamoxifen would have been useful in treating all the breast conditions because progesterone which has been shown to be useful by Jarvis patent in treating breast condition has not been known to treat every single benign breast condition. Fentiman demonstrate oral administration of tamoxifen is useful in treating mastalgia and is cited for teaching that mastalgia can be cyclical. Pujol teaches the percutaneous application to the breast of dosages of 4-OHT of 0.5 mg/day (0.25 mg/breast) or 1.0 mg/day (0.5 mg/breast). Applicants' have shown that such doses are ineffective against mastalgia. See, e.g. Example 4, paragraphs [0063] - [0065] and Tables 8 and 9. Accordingly, it would not have been obvious to one having ordinary skill in the art at the time of the invention from the prior art teachings that a composition comprising 4-OHT as the sole therapeutically active ingredient to treat mastalgia would be useful in treating mastalgia, a species of the benign breast conditions specifically at the claimed concentration of 1.5 mg/day of 4-OHT.

The claims are allowable over the closest art of record because they do not teach or disclose the claimed method of treatment of mastalgia comprising administering percutaneously to the breasts of a patient having mastalgia a composition comprising 4-OH tamoxifen as the sole therapeutically active ingredient at a dose of at least 1.5 mg/day of 4-hydroxy tamoxifen.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627